

Amendments to the Specification

Please replace the paragraph beginning at page 1, line 13, with the following rewritten paragraph:

Methods utilizing mass spectrometry for the analysis of a target polypeptide have been taught wherein the polypeptide is first solubilized in an appropriate solution or reagent system. The type of solution or reagent system, e.g., comprising an organic or inorganic solvent, will depend on the properties of the polypeptide and the type of mass spectrometry performed and are well-known in the art (see, e.g. Vorm et al. (1994) Anal. Chem. 66:3281 (for MALDI) and Valaskovic et al. (1995) Anal. Chem. 67:3802 (for ESI)). Mass spectrometry of peptides is further disclosed, e.g. in WO 93/24834 by Chait et al.

Please replace the paragraph, as previously amended on June 16, 2003 and November 29, 2004, beginning at page 19, line 2, with the following rewritten paragraph:

Figure 1 is a representation of derived data which characterizes a disease specific marker having a particular sequence, ~~(SEQ ID NO:1)~~ SEQ ID NO:1, useful in evidencing and categorizing at least one particular disease state[[.]] ; ~~and Each patient listed in the data table shows the presence of the disease specific marker (SEQ~~

~~ID NO.1) in their serum.~~

Figure 2 is the characteristic profile derived via SELDI/TOF MS of the disease specific marker ~~of Figure 1, SEQ ID NO:1. SEQ ID NO:1~~ is shown.

Please replace the paragraph beginning at page 21, line 7, with the following rewritten paragraph:

Spotting was then performed, for example upon a Gold Chip in the following manner:

1. spot 2µl of sample onto each ~~[[spot]]~~ chip
2. let sample partially dry
3. spot 1µl of ~~[[matrx]]~~ matrix, and let air dry.

Please replace the paragraph beginning at page 21, line 12, with the following rewritten paragraph:

HiQ Anion Exchange Mini Column Protocol

- 1) Dilute sera in sample/running buffer;
- 2) Add HiQ resin to column and remove any air bubbles;
- 3) Add ultrafiltered (UF) ~~[[Uf]]~~ water to aid in column packing;
- 4) Add sample/running buffer to equilibrate column;
- 5) Add diluted sera;
- 6) Collect all the flow-through fraction in ~~Eppendorf~~

- EPPENDORF tubes until level is at resin;
- 7) Add sample/running buffer to wash column;
 - 8) Add ~~elusion~~ elution buffer and collect ~~elusion~~ elution in ~~Eppendorf~~ EPPENDORF tubes.

Please replace the paragraph beginning at page 22, line 2, with the following rewritten paragraph:

Sample/Running buffers: including but not limited to Bicine buffers of various molarities, pH's, NaCl content, ~~Bis-Tris~~ BIS-TRIS buffers of various molarities, pH's, NaCl content, Diethanolamine of various molarities, pH's, NaCl content, Diethylamine of various molarities, pH's, NaCl content, Imidazole of various molarities, pH's, NaCl content, Tricine of various molarities, pH's, NaCl content, Triethanolamine of various molarities, pH's, NaCl content, [[Tris]] TRIS of various molarities, pH's, NaCl content.

Please replace the paragraph beginning at page 24, line 1, with the following rewritten paragraph:

HiS Cation Exchange Mini Column Protocol

- 1) Dilute sera in sample/running buffer;
- 2) Add HiS resin to column and remove any air bubbles;
- 3) Add ultrafiltered (UF) [[Uf]] water to aid in column

packing;

- 4) Add sample/running buffer to equilibrate column for sample loading;
- 5) Add diluted sera to column;
- 6) Collect all flow through fractions in ~~Eppendorf~~ EPPENDORF tubes until level is at resin[[]] ;
- 7) Add sample/running buffer to wash column[[]] ;
- 8) Add ~~elution~~ elution buffer and collect ~~elution~~ elution in ~~Eppendorf~~ EPPENDORF tubes.

Please replace the paragraph beginning at page 24, line 15, with the following rewritten paragraph:

Sample/Running buffers: including but not limited to Bicine buffers of various molarities, pH's, NaCl content, ~~Bis-Tris~~ BIS-TRIS buffers of various molarities, pH's, NaCl content, Diethanolamine of various molarities, pH's, NaCl content, Diethylamine of various molarities, pH's, NaCl content, Imidazole of various molarities, pH's, NaCl content, Tricine of various molarities, pH's, NaCl content, Triethanolamine of various molarities, pH's, NaCl content, [[Tris]] TRIS of various molarities, pH's, NaCl content.

Please replace the paragraph beginning at page 27, line 6, with the following rewritten paragraph:

For example, Serum (20ml) was (diluted 5-fold with phosphate buffered saline) concentrated by centrifugation through a YM3 MICROCON spin filter ~~(Amicon)~~ (AMICON) for 20 min at 10,000 RPM at 4°C in a Beckman MICROCENTRIFuge R model bench top centrifuge. The filtrate was discarded and the retained solution, which contained the two peptides of interest, was analyzed further by tandem mass spectrometry to deduce their amino acid sequences. Tandem mass spectrometry was performed at the University of Manitoba's (Winnipeg, Manitoba, Canada) mass spectrometry laboratory using the procedures that are well known to practitioners of the art.

Please replace the paragraph beginning at page 28, line 11, with the following rewritten paragraph:

The specific disease markers which are analyzed according to the method of the invention are released into the circulation and may be present in the blood or in any blood product, for example plasma, serum, cytolyzed blood, e.g. by treatment with hypotonic buffer or detergents and dilutions and preparations thereof, and other body fluids, e.g. [[CSF]] cerebrospinal fluid (CSF), saliva, urine, lymph, and the like. The presence of each marker is determined using antibodies specific for each of the markers and

detecting specific binding of each antibody to its respective marker. Any suitable direct or indirect assay method may be used to determine the level of each of the specific markers measured according to the invention. The assays may be competitive assays, sandwich assays, and the label may be selected from the group of well-known labels such as radioimmunoassay, fluorescent or chemiluminescence immunoassay, or immunoPCR technology. Extensive discussion of the known immunoassay techniques is not required here since these are known to those of ~~skilled~~ skill in the art. See Takahashi et al. (Clin Chem 1999; 45(8): 1307) for S100B assay.